\* \* \* \* \* \* \* \* STN Columbus

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=> file ca, wpids, uspat

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TOTAL

FULL ESTIMATED COST

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FILE 'USPATFULL' ENTERED AT 11:02:49 ON 08 APR 1997 CA INDEXING COPYRIGHT (C) 1997 AMERICAN CHEMICAL SOCIETY (ACS)

=> s lys-pro-val

160 FILE CA L1

L267 FILE WPIDS

68 FILE USPATFULL

TOTAL FOR ALL FILES

295 LYS-PRO-VAL

=> s inflammat?

L5 69490 FILE CA

18898 FILE WPIDS L6

L7 20715 FILE USPATFULL

TOTAL FOR ALL FILES

109103 INFLAMMAT?

=> s 14 and 18

L9 7 FILE CA

L108 FILE WPIDS

L1118 FILE USPATFULL

TOTAL FOR ALL FILES

L1233 L4 AND L8

=> dup rem 112

PROCESSING COMPLETED FOR L12

L13 30 DUP REM L12 (3 DUPLICATES REMOVED)

=> d 1-30 bib, abs

L13 ANSWER 1 OF 30 USPATFULL AN

97:26904 USPATFULL

Non-crosslinked procein particles for therapeutic and diagnostic TI Yen, Richard C. K., Glendora, CA, United States IN Hemosphere, Inc., Irvine, CA, United States (U.S. corporation) PA ΡI US 5616311 970401 ΑI US 94-212546 940314 (8) Continuation-in-part of Ser. No. US 93-69831, filed on 1 Jun 1993, RLI now abandoned And Ser. No. US 92-959560, filed on 13 Oct 1992, now patented, Pat. No. US 5308620 which is a continuation-in-part of Ser. No. US 91-641720, filed on 15 Jan 1991, now abandoned DT Utility EXNAM Primary Examiner: Lovering, Richard D. LREP Townsend & Townsend & Crew CLMN Number of Claims: 26 ECL Exemplary Claim: 1,26 DRWN No Drawings LN.CNT 2585 Albumin particles in the nanometer and micrometer size range in an AB aqueous suspension are rendered stable against resolubilization without the aid of a crosslinking agent and without denaturation, by the incorporation of hemoglobin in the particle composition. Particles which are primarily hemoglobin in the nanometer and micrometer size range in an aqueous suspension are rendered stable against aggregation by the incorporation of either albumin, surface active agents or gelatin. L13 ANSWER 2 OF 30 USPATFULL AN97:8000 USPATFULL TITumor necrosis factor muteins Banner, David, Basle, Switzerland IN Lesslauer, Werner, Riehen, Switzerland Lotscher, Hansruedi, Mohlin, Switzerland Stuber, Dietrich, Grenzach-Wyhlen, Germany, Federal Republic of Hoffmann-La Roche Inc., Nutley, NJ, United States (U.S. PA corporation) PIUS 5597899 970128 ΑI US 94-217529 940324 (8) PRAI EP 93-810224 930329 DTUtility EXNAM Primary Examiner: Wax, Robert A.; Assistant Examiner: Carlson, Karen Cochrane LREP Johnston, George W.; Epstein, William H.; Smith, Catherine R. CLMN Number of Claims: 10 ECL Exemplary Claim: 1 13 Drawing Figure(s); 12 Drawing Page(s) DRWN LN.CNT 1506 CAS INDEXING IS AVAILABLE FOR THIS PATENT. Human TNF muteins having higher binding affinity for human p75-TNF ABreceptor than for human p55-TNF receptor include muteins having at least one different amino acid relative to wild-type human TNF at

or 147 of the wild-type amino acid sequence.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L13 ANSWER 3 OF 30 WPIDS COPYRIGHT 1997 DERWENT INFORMATION LTD AN 97-055459 [06] WPIDS

a position corresponding to position 33, 65, 67,  $\overline{75}$ , 87, 143, 145

```
DNC
       C97-018478
      Drug for promotion or stimulation of hair growth - contains tri
  TI
      peptide comprising lysine, proline and valine.
 DC
      MAHE, Y
 IN
 PA
       (OREA) L'OREAL SA
 CYC
 PΙ
      JP 08301729 A 961119 (9706)*
                                          gg 8
      FR 2733421 A1 961031 (9706)
                                          16 pp
      EP 759292
                  A1 970226 (9714) FR
                                          11 pp
          R: DE ES FR GB IT
      JP 08301729 A JP 96-108203 960426; FR 2733421 A1 FR 95-5158 950428;
 ADT
      EP 759292 A1 EP 96-400653 960327
 PRAI FR 95-5158
                     950428
 AN
      97-055459 [06]
                       WPIDS
      JP08301729 A UPAB: 970205
 AB
      Drug for the promotion or stimulation of hair growth and/or the
      prevention of hair loss contains at least one peptide contg. a
      tripeptide of
                     ***Lys*** - ***Pro*** ~ ***Val***
                                                               (LPV) or its
      functional equivalent except those in which the histidine residue is
      present just upstream of the LPV sequence.
           Also claimed are a drug for the treatment of the
      ***inflammatory*'**
                          stage of depilation contg. the above peptide,
      and a method for treating hair and/or the scalp in which a compsn.
      of the above drug is applied on the hair and/or the scalp and stood
      and then rinsed.
           ADVANTAGE - The drug is partic. used for the application in the
      ***inflammatory*** stage of depilation.
           In an example, the effect of Ac-LPV-NH2 and alpha-melanin cell
      stimulating hormone on the retention and the length of hair vesicle
      was examined. The average length was 2.40 cm after 12 days when
      Williams medium E and 10 mM Ac-LPV-NH2 were used, compared to 1.79
      cm for a control using no peptide.
     Dwq.0/0
     ANSWER 4 OF 30 USPATFULL
L13
AN
        96:111445 USPATFULL
TI
       Peptides
       Ferreira, Sergio H., Est. Sao Paulo, Brazil
IN
       Bristow, Adrian F., Hertfordshire, England
       Poole, Stephen, London, England
       British Technology Group Limited, London, England (non-U.S.
PA
       corporation)
ΡI
       US 5580855 961203
ΑI
       US 94-330845 941027 (8)
       Continuation of Ser. No. US 93-95856, filed on 23 Jul 1993, now
RLI
       patented, Pat. No. US 5389615 which is a continuation of Ser. No.
       US 89-438404, filed on 20 Dec 1989, now abandoned
PRAI
       GB 88-7427 880328
       GB 88-28833 881209
DT
       Utility
       Primary Examiner: Weimar, Elizabeth C.; Assistant Examiner:
EXNAM
       Marshall, S. G.
LREP
       Nixon & Vanderhye
CLMN
       Number of Claims: 7
ECL
       Exemplary Claim: 1
DRWN
       14 Drawing Figure(s); 9 Drawing Page(s)
LN.CNT 811
```

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

Peptides, the C-terminal amides thereof and the pharmaceutically ABacceptable salts of the said peptides and amides are useful in the prevention and treatment of pain.

### CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L13 ANSWER 5 OF 30 USPATFULL

ΑN 96:72766 USPATFULL

Assay for determinig TNF or IL-1 convertase activity TI IN

Kriegler, Michael, San Francisco, CA, United States

Nitecki, Danute E., Berkeley, CA, United States

Cetus Oncology Corporation, Emeryville, CA, United States (U.S. PΑ corporation)

PΙ US 5545518 960813

ΑI US 95-385434 950208 (8)

Division of Ser. No. US 93-53558, filed on 26 Apr 1993, now RLIpatented, Pat. No. US 5422425 which is a continuation of Ser. No. US 90-562720, filed on 6 Aug 1990, now abandoned

DTUtility

Primary Examiner: Fleisher, Mindy; Assistant Examiner: Degen, EXNAM Nancy J.

Pochopien, Donald J.; Savereide, Paul B.; Blackburn, Robert P. LREP

CLMN Number of Claims: 12

ECLExemplary Claim: 1

DRWN 5 Drawing Figure(s); 3 Drawing Page(s)

LN.CNT 824

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

Compositions and methods are described for identifying inhibitors AB of mature protein hormone formation from a prohormone, and prophylactic and therapeutic uses of the inhibitors for treating diseases associated with elevated levels of the mature hormones, particulary sepsis, and autoimmune diseases.

## CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L13 ANSWER 6 OF 30 USPATFULL

AN 96:19200 USPATFULL

ΤI Peptidase inhibitors

Kolb, H. Michael, Cincinnati, OH, United States IN Burkhart, Joseph P., West Chester, OH, United States Jung, Michel J., Pfaffenhoffen, France Gerhart, deceased, Fritz E., late of Kehl Leutesheim, Germany, Federal Republic of by Jutta Gerhart, legal representative Giroux, Eugene L., Cincinnati, OH, United States Neises, Bernhard, Offenburg-Griesheim, Germany, Federal Republic

Schirlin, Daniel G., Lampertheim, France

Merrell Pharmaceuticals Inc., Cincinnati, OH, United States (U.S. PA corporation)

PΙ US 5496927 960305

US 94-248847 940525 (8) ΑI

Continuation of Ser. No. US 93-102522, filed on 4 Aug 1993, now RLI abandoned which is a continuation of Ser. No. US 92-980141, filed on 23 Nov 1992, now abandoned which is a continuation of Ser. No. US 90-540033, filed on 19 Jun 1990, now abandoned which is a continuation-in-part of Ser. No. US 89-372162, filed on 27 Jun 1989; now abandoned which is a continuation of Ser. No. US

88-267758, filed on 1 Nov 1988, now abandoned which is a continuation of Ser. No. US 86-874721, filed on 16 Jun 1986, now abandoned which is a continuation-in-part of Ser. No. US 85-697987, filed on 4 Feb 1985, now abandoned

DTUtility

Primary Examiner: Warden, Jill; Assistant Examiner: Huff, Sheela EXNAM

LREP Boudreaux, William R. CLMN Number of Claims: 7 ECL Exemplary Claim: 1 No Drawings DRWN

LN.CNT 2467

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

This invention relates to analogs of peptidase substrates in which AB the amide group containing the scissile amide bond of the substrate peptide has been replaced by an activated electrophilic ketone moiety. These analogs of the peptidase substrates provide specific enzyme inhibitors for a variety of proteases, the inhibition of which will have useful physiological consequences in a variety of disease states.

# CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L13 ANSWER 7 OF 30 USPATFULL

AN 96:7652 USPATFULL

TI TNF-muteins

Lesslauer, Werner, Riehen, Switzerland IN Lotscher, Hansruedi, Molin, Switzerland

Stuber, Dietrich, Grenzach-Wyhlen, Germany, Federal Republic of

Hoffmann-La Roche Inc., Nutley, NJ, United States (U.S. corporation)

PΙ US 5486463 960123

ΑI US 93-41648 930401 (8)

PRAI EP 92-810249 920402

DTUtility

PA

Primary Examiner: Draper, Garnette D.; Assistant Examiner: EXNAM Carlson, K. Cochrane

Gould, George M.; Epstein, William H.; Picut, Catherine A. LREP

CLMN Number of Claims: 27 ECLExemplary Claim: 1

DRWN 17 Drawing Figure(s); 15 Drawing Page(s)

LN.CNT 1464

AN

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

The present invention is directed to a human Tumor Necrosis Factor AΒ mutein or a pharmaceutically acceptable salt thereof having selective binding affinity for the human p55-Tumor-Necrosis-Factor-Receptor characterized in that the amino acid sequence of human Tumor Necrosis Factor is changed at least at position 86 having a threonine instead of a serine residue, a DNA sequence coding for such a mutein, a vector comprising such a DNA sequence, and a host cell transformed by such a vector.

## CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L13 ANSWER 8 OF 30 USPATFULL

95:50249 USPATFULL

Methods for the identification of cytokine convertase inhibitors TIIN

Kriegler, Michael, San Francisco, CA, United States

Nitecki, Danute E., Berkeley, CA, United States Cetus Oncology Corporation, Emeryville, CA, United States (U.S. PA corporation) PΙ US 5422425 950606 US 93-53558 930426 (8) ΑI Continuation of Ser. No. US 90-562720, filed on 6 Aug 1990, now RLI abandoned DT Utility EXNAM Primary Examiner: Russel, Jeffrey E. Pochopien, Donald J.; Savereide, Paul B.; Blackburn, Robert P. LREP CLMNNumber of Claims: 2 ECL Exemplary Claim: 1 DRWN 5 Drawing Figure(s); 3 Drawing Page(s) LN.CNT 696 CAS INDEXING IS AVAILABLE FOR THIS PATENT. Compositions and methods are described for identifying inhibitors AΒ of mature protein hormone formation from a prohormone, and prophylactic and therapeutic uses of the inhibitors for treating diseases associated with elevated levels of the mature hormones, particulary sepsis, and autoimmune diseases. CAS INDEXING IS AVAILABLE FOR THIS PATENT. ANSWER 9 OF 30 USPATFULL L13 AN 95:49929 USPATFULL TITNF-muteins IN Fiers, Walter, Destelbergen, Belgium Tavernier, Jan, Balegem, Belgium Van Ostade, Xaveer, Antwerp, Belgium Hoffmann-La Roche Inc., Nutley, NJ, United States (U.S. PA corporation) PΙ US 5422104 950606 AΙ US 91-794400 911120 (7) PRAT EP 90-810901 901121 Utility DTPrimary Examiner: Draper, Garnette D.; Assistant Examiner: EXNAM Carlson, K. Cochrane LREP Gould, George M.; Epstein, William H.; Picut, Catherine A. CLMN Number of Claims: 4 ECL Exemplary Claim: 1 24 Drawing Figure(s); 16 Drawing Page(s) DRWN LN.CNT 1778 CAS INDEXING IS AVAILABLE FOR THIS PATENT. It is an object of this invention to provide a human Tumor AB Necrosis Factor mutein or a pharmaceutically acceptable salt thereof characterized in that the TNF sequence is changed by a deletion, insertion, substitution or combinations thereof, of one or more amino acids so that the mutein shows a significant difference between its binding affinity to the human p75-Tumor-Necrosis-Factor-Receptor and to the human p55-Tumor-Necrosis-Factor-Receptor. The invention also includes DNA sequences coding for such muteins, vectors comprising such DNA sequences, host cells transformed with such vectors and a process for the production of such muteins employing such transformed host cells and pharmaceutical compositions containing such muteins and

their use for the treatment of illnesses, for example cancer.

```
L13
      ANSWER 10 OF 30 USPATFULL
 AN
        95:13848 USPATFULL
        Peptides and pharmaceutical composition thereof in the treatment
 TI
        of pain
        Ferreira, Sergio H., Est. Sao Paulo, Brazil
 ΙN
        Bristow, Adrian F., Hertfordshire, England
        Poole, Stephen, London, England
        British Technology Group Ltd., London, England (non-U.S.
 PA
        corporation)
 PΙ
        US 5389615
                   950214
        WO 8909226 891005
 AΙ
        US 93-95856 930723 (8)
        WO 89-GB319
                     890328
               891220 PCT 371 date
               891220 PCT 102(e) date
        Continuation of Ser. No. US 89-438404, filed on 20 Dec 1989, now
 RLI
        abandoned
 PRAI
        GB 88-7427 880328
        GB 88-28833 881209
 DT
        Utility
        Primary Examiner: Hill, Jr., Robert J.; Assistant Examiner:
 EXNAM
        Marshall, S. G.
LREP
        Nixon & Vanderhye
CLMN
       Number of Claims: 14
ECL
        Exemplary Claim: 1
        9 Drawing Figure(s); 9 Drawing Page(s)
DRWN
LN.CNT 831
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       Peptides and pharmaceutical composition thereof useful in the
AΒ
       treatment of pain.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
L13
     ANSWER 11 OF 30 USPATFULL
AN
       94:86182 USPATFULL
ΤI
       Method for preparing vaccine for dental caries and vaccinal
       compositions for dental caries used as nasal drop
       Koga, Toshihiko, Tokyo, Japan
IN
       Okahashi, Nobuo, Komae, Japan
       Takahashi, Ichiro, Yokohama, Japan
       Shibuya, Koji, Kanagawa, Japan
       Ohta, Hirotaka, Kanagawa, Japan
       Lion Corporation, Tokyo, Japan (non-U.S. corporation)
PA
       National Institute of Health, Tokyo, Japan (non-U.S. corporation)
PΙ
       US 5352450
                  941004
AΙ
       US 90-529602 900529 (7)
PRAI
       JP 89-1137025 890529
       JP 89-1207700 890809
DT
       Utility
      Primary Examiner: Nucker, Christine M.; Assistant Examiner:
EXNAM
       Sidberry, Hazel F.
LREP
       Burns, Doane, Swecker & Mathis
CLMN
       Number of Claims: 4
ECL
       Exemplary Claim: 1
DRWN
       2 Drawing Figure(s); 2 Drawing Page(s)
LN.CNT 910
      A method for preparing a vaccine for dental caries comprises the
AB
```

step of culturing a variant which is obtained by integrating a protein antigen (PAc)-expressing gene into the chromosomal gene of a Streptococcus mutans GS-5 strain to obtain the protein antigen, the protein antigen being produced on the surface of cells of oral Streptococcus mutans or it being extracellularly produced by the microorganism and having a molecular weight ranging from about 170,000 to 220,000. Streptococcus mutans GS-5 (K-3), in which a protein antigen-expressing gene is integrated into the chromosomal gene thereof, has an ability of producing the protein antigen on the surface of the cells or extracellularly. A preventive vaccine composition for dental caries for nasal drops comprises the protein antigen thus produced by the strain: Streptcoccus mutans, the vaccine being intranasally administered. The method makes it possible to enhance the yield of PAc and to simplify processes for purifying PAc. The vaccine composition makes-it possible to internally easily absorb the protein antigen, PAc, in high efficiency and it also makes it possible to effectively increase the antibody titer observed after the administration thereof.

```
L13
     ANSWER 12 OF 30 USPATFULL
AN
       94:11399 USPATFULL
       Synthetic tetrapeptides for the prevention of schistosome parasite
TI
       infection
       McKerrow, James H., San Francisco, CA, United States
IN
       Cohen, Fred E., San Francisco, CA, United States
       The Regents of the University of California, Oakland, CA, United
PΑ
       States (U.S. corporation)
PΙ
       US 5284829 940208
AΙ
       US 91-798565 911126 (7)
DT
       Utility
EXNAM
       Primary Examiner: Griffin, Ronald W.
LREP
       Robbins, Berliner & Carson
       Number of Claims: 16
CLMN
ECL
       Exemplary Claim: 1
       4 Drawing Figure(s); 3 Drawing Page(s)
DRWN
LN.CNT 1218
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       The invention relates to synthetic tetrapeptides that contain a
       peptide blocking group at the amino terminus and an enzyme
       inhibitor at the carboxy terminus, and their use in the prevention
       of schistosome parasite infection.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
     ANSWER 13 OF 30 CA COPYRIGHT 1997 ACS
L13
AN
     120:261705 CA
    Antiinflammatory influences of .alpha.~MSH molecules: central
TI
    neurogenic and peripheral actions
    Macaluso, A.; McCoy, D.; Ceriani, G.; Watanabe, T.; Biltz, J.;
ΑU
    Catania, A.; Lipton, J. M.
    Southwest. Med. Cent., Univ. Texas, Dallas, TX, 75235-9040, USA
```

.alpha.-MSH (.alpha.-MSH1-13) and its COOH-terminal tripeptide

.alpha.-MSH11-13 ( \*\*\*Lys\*\*\* - \*\*\*Pro\*\*\* - \*\*\*Val\*\*\* ) inhibit

J. Neurosci. (1994), 14(4), 2377-82

CODEN: JNRSDS; ISSN: 0270-6474

CS. SO .

DT

LA

AB

Journal

English

when administered systematically. Recent \*\*\*inflammation\*\*\* evidence indicates that .alpha.-MSH1-13 can likewise inhibit \*\*\*inflammation\*\*\* in the skin solely via an action within the brain. Because of the potential importance of this discovery to understanding the control of \*\*\*inflammation\*\*\* and because .alpha.-MSH mols. might be useful for treatment of \*\*\*inflammation\*\*\* , expts. were performed to learn more about the mechanisms of action of these peptides. In tests on \*\*\*inflammation\*\*\* induced in the mouse ear by intradermal injections of recombinant human interleukin-1.beta., .alpha.-MSH1-13 administered intracerebroventricularly effectively reduced \*\*\*inflammation\*\*\* . This effect of centrally administered .alpha.-MSH1-13 was inhibited by systemic injection of the nonspecific .beta.-adrenergic receptor blocker propranolol and by administration of a specific .beta.2-adrenergic receptor antagonist: the effect was not altered by blockade of cholinergic, .alpha.-adrenergic, or .beta.1-adrenergic receptors. In mice with induced in a hind paw and with the spinal cord \*\*\*inflammation\*\*\* transected, the antiinflammatory effect of centrally administered .alpha.-MSH1-13 was prevented, indicating that intact descending neuronal pathways are required for the antiinflammatory influence of the central peptide. Systemic injection of .alpha.-MSH1-13 in animals with spinal cord transection had a smaller and later antiinflammatory effect, which suggests that the mol. also has an action, albeit lesser, in the periphery. However, .alpha.-MSH11-13 injected i.p. had marked antiinflammatory activity in animals with spinal cord transection. The combined evidence indicates that .alpha.-MSH1-13 has both central and peripheral sites of action in modulation of \*\*\*inflammation\*\*\*; the central effects of .alpha.-MSH1-13 are mediated by pathways that involve peripheral .beta.2-adrenergic receptors; the antiinflammatory/antipyretic message sequence of .alpha.-MSH1-13, .alpha.-MSH11-13, has potent antiinflammatory activity when given systematically, activity that does not require intact spinal cord pathways.

- L13 ANSWER 14 OF 30 CA COPYRIGHT 1997 ACS
- AN 121:27316 CA
- TI Binding of anti- \*\*\*inflammatory\*\*\* .alpha.-melanocytestimulating-hormone peptides and proinflammatory cytokines to receptors on melanoma cells
- AU Lyson, Krzysztof; Ceriani, Giuliana; Takashima, Akira; Catania, Anna; Lipton, James M.
- CS Dep. Physiol., Univ. Tex. Southwest. Med. Cent., Dallas, TX, 75235-9068, USA
- SO NeuroImmunoModulation (1994), 1(2), 121-6 CODEN: NROIEM
- DT Journal
- LA English
- AB .alpha.-MSH (.alpha.-MSH1-13), a peptide derived from proopiomelanocortin, has remarkable anti- \*\*\*inflammatory\*\*\* and antipyretic activities. This peptide and a tripeptide that forms the C-terminal portion of the mol. (.alpha.-MSH11-13; \*\*\*Lys\*\*\* \*\*\*Pro\*\*\* \*\*\*Val\*\*\* ) inhibit \*\*\*inflammation\*\*\* when given centrally or peripherally. Because of the similarity in their actions, the tripeptide has been presumed to be the amino acid message sequence underlying the effects of .alpha.-MSH1-13. To test the possibility that the 2 peptides occupy the same receptors, competitive binding expts. were performed with B16 mouse melanoma

cells that are known to have .alpha.-MSH1-13 receptors. In these expts., .alpha.-MSH1-13 did not inhibit binding of a radiolabeled .alpha.-MSH1-13 analog. This finding suggests that .alpha.-MSH1-13 and .alpha.-MSH1-13 exert their antiinflammatory/antipyretic/anticy tokine effects via stimulation of sep. receptors. Because .alpha.-MSH inhibits the effects of several cytokines including \*\*\*inflammation\*\*\* caused by interleukin (IL)-6 and IL-8, the capacity of these cytokines to compete for .alpha.-MSH binding sites was tested. There was no evidence that these proinflammatory cytokines bind to .alpha.-MSH receptors on murine melanoma cells. Although further tests with host cells involved in \*\*\*inflammation\*\*\* are required, the latter result is the first evidence that the mechanism of anticytokine action of .alpha.-MSH does not depend upon peptide/cytokine competition for binding sites.

L13 ANSWER 15 OF 30 USPATFULL

AN 93:61018 USPATFULL

TI CDNAS coding for members of the carcinoembryonic antigen family

IN Barnett, Thomas R., East Haven, CT, United States
Elting, James J., Madison, CT, United States
Kamarck, Michael E., Bethany, CT, United States

Kretschmer, Axel W., Wulfrath, Germany, Federal Republic of

PA Molecular Diagnostics, Inc., West Haven, CT, United States (U.S. corporation)

PI US 5231009 930727

AI US 91-760031 910913 (7)

Division of Ser. No. US 88-274107, filed on 2 Nov 1988, now patented, Pat. No. US 5122599 which is a continuation-in-part of Ser. No. US 88-207678, filed on 15 Jun 1988, now abandoned which is a continuation-in-part of Ser. No. US 87-60031, filed on 19 Jun 1987, now abandoned which is a continuation-in-part of Ser. No. US 87-16683, filed on 19 Feb 1987, now abandoned which is a continuation-in-part of Ser. No. US 86-896361, filed on 13 Aug 1986, now abandoned

DT Utility

EXNAM Primary Examiner: Moskowitz, Margaret; Assistant Examiner: Fleisher, Mindy B.

LREP Sprung Horn Kramer & Woods

CLMN Number of Claims: 2 ECL Exemplary Claim: 1

ECL Exemplary Claim: 1
DRWN 4 Drawing Figure(s); 1 Drawing Page(s)

LN.CNT 4434

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

Anucleic acid comprising a base sequence which codes for a CEA family member peptide sequence or nucleic acids having a base sequence hybridizable therewith, replicable recombinant cloning vehicles having an insert comprising such nucleic acid, cells transfected, infected or injected with such cloning vehicles, polypeptides expressed by such cells, synthetic peptides derived from the coding sequence of CEA family member nucleic acids, antibody preparations specific for such polypeptides, immunoassays for detecting CEA family members using such antibody preparations and nucleic acid hybridization methods for detecting CEA family member nucleic acid sequences using a nucleic acid probe comprising the above described nucleic acid.

```
L13
      ANSWER 16 OF 30 CA COPYRIGHT 1997 ACS
 AN
      119:217622 CA
      Inhibition of IL-1.beta.-induced peripheral ***inflammation***
 TI
      by peripheral and central administration of analogs of the
      neuropeptide .alpha.-MSH
      Watanabe, Tatsuo; Hiltz, Melanie E.; Catania, Anna; Lipton, James M.
 AU
      Sch. Med., Yamaguchi Univ., Ube, 755, Japan
 CS
     Brain Res. Bull. (1993), 32(3), 311-14
 SO
      CODEN: BRBUDU; ISSN: 0361-9230
DT
      Journal
LA
     English
     Interleukin-1 (IL-1) is a proinflammatory cytokine.
AΒ
      .alpha.-MSH(1-13) mols. inhibit ***inflammation*** induced by
     cytokines, other mediators of ***inflammation*** , and by
     peripheral irritants. D-Valine substitution in the
     antiinflammatory/antipyretic message sequence [.alpha.-MSH(11-13),
     ***Lys*** - ***Pro*** - ***Val*** ] of .alpha.-MSH(1-13)
     increases the activity of the tripeptide. The authors' aim was to
     learn if D-valine substitution also enhances the antiinflammatory
     activity of the entire .alpha.-MSH(1-13) mol. and to det. if an
     antipyretic D-valine-substituted .alpha.-MSH(8-13) mol. is also
     antiinflammatory. I.p. injection of .alpha.-MSH(1-13) and of
     [D-Val13].alpha.-MSH(1-13) caused dose-related suppression of ear
     edema induced in mice by intradermal injection of IL-1.beta.; the 2
     mols. were equipotent. [D-Val13].alpha.-MSH(8-13) likewise
     inhibited
                 ***inflammation*** , but the potency was less than that
     of the larger mols. Intracerebroventricular injections of
     [D-Val13].alpha.-MSH(1-13) and of the unsubstituted mol. were
     equipotent in reducing ***inflammation***; the
     [D-Val13].alpha.-MSH(8-13) mol. was less effective.
                                                          The results
     support the idea that the .alpha.-MSH(1-13) mol. inhibits
     ***inflammation*** and suggest that the L-conformation of
     .alpha.-MSH(1-13) is maximally effective with regard to its
     antiinflammatory activity. The results with .alpha.-MSH(8-13) are
     consistent with previous findings of lesser antihost response
     activity of .alpha.-MSH fragments that contain the COOH-terminal
                 ***Lys*** - ***Pro*** - ***Val***
     tripeptide
L13
     ANSWER 17 OF 30 USPATFULL
AN
       92:86953 USPATFULL
       Antipyretic and anti- ***inflammatory***
TI
                    ***val*** compositions and method of use
       ***pro***
       Lipton, James M., 10662 Royal Springs Dr., Dallas, TX, United
ΙN
       States 75229
PΙ
       US 5157023 921020
ΑI
       US 91-672965 910321 (7)
       Division of Ser. No. US 88-229331, filed on 5 Aug 1988, now
RLI
       patented, Pat. No. US 5028592 which is a continuation of Ser. No.
      US 87-76625, filed on 23 Jul 1987, now abandoned which is a
       continuation-in-part of Ser. No. US 86-894910, filed on 8 Aug
       1986, now abandoned which is a continuation-in-part of Ser. No. US
       84-643023, filed on 21 Aug 1984, now abandoned
DT
       Utility
EXNAM
       Primary Examiner: Lee, Lester L.
      Arnold, White & Durkee
LREP
CLMN
      Number of Claims: 8
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ECL

DRWN

Exemplary Claim: 1

2 Drawing Figure(s); 1 Drawing Page(s)

LN.CNT 708

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

An antipyretic tripeptide, having the amino acid sequence lysine-proline-valine, and a method for utilizing the tripeptide to reduce fever and \*\*\*inflammation\*\*\* in mammals are disclosed. The tripeptide can either be isolated from natural sources or chemically synthesized. A "protected" tripeptide having greater antipyretic potency and duration of action is also disclosed. The "protected" tripeptide contains an acyl group, such as an acetyl or a dibenzyl oxy carboxyl group, at its amino terminals and is amidated or esterified at its carboxyl terminals. Further, improved antipyretic potency and direction of action can be achieved through the co-administration of copper salts with the tripeptide.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

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L13 ANSWER 18 OF 30 CA COPYRIGHT 1997 ACS DUPLICATE 1
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AN 116:34564 CA

TI Preparation of antipyretic and antiinflammatory peptides

IN Lipton, James M.

PA USA

SO U.S., 9 pp. Cont. of U.S. Ser. No. 76,625, abandoned. CODEN: USXXAM

PI US 5028592 A 910702

AI US 88-229331 880805

PRAI US 84-643023 840821 US 86-894910 860808

US 87-76625 870723

DT Patent

LA English

Peptides having 3-13 amino acids and contg. the \*\*\*Lys\*\*\* \*\*\*Pro\*\*\* - \*\*\*Val\*\*\* sequence are antipyretics and
\*\*\*inflammation\*\*\* inhibitors. \*\*\*Lys\*\*\* - \*\*\*Pro\*\*\* \*\*\*Val\*\*\* and its protected derivs. were prepd. by known methods.
Ac2- \*\*\*Lys\*\*\* - \*\*\*Pro\*\*\* - \*\*\*Val\*\*\* -NH2 (1.25 .mu.g/kg;
i.v.) reduced in rabbits the histamine-induced blue "weal"
formation, which is indicative of antiinflammatory activity (Sparrow and Wilhelm, 1957). Coadministration of Cu salts increased the antipyretic potency of the tripeptide.

L13 ANSWER 19 OF 30 WPIDS COPYRIGHT 1997 DERWENT INFORMATION LTD

AN 91-044974 [07] WPIDS

DNC C91-019064

TI New hybrid protein contg. TNF and leukokinin fragment - has therapeutic and prophylactic use e.g. against infections, tumours, transplant rejection and \*\*\*inflammation\*\*\*

DC B04 D16

IN DAUM, L; DOERER, T; EMLING, F; HILLEN, H; MOELLER, A; DOERPER, T

PA (BADI) BASF AG

CYC 16

PI DE 3925183 A 910207 (9107)\* WO 9101998 A 910221 (9110)

RW: AT BE CH DE DK ES FR GB IT LU NL SE

W: CA JP US

EP 485407 A1 920520 (9221) DE 18 pp

R: AT BE CH DE ES FR GB IT LI NL

JP 04507241 W 921217 (9305) 7

ADT DE 3925183 A DE 89-3025183 890729; EP 485407 A1 EP 90-910668 900720, WO 90-EP1190 900720; JP 04507241 W JP 90-509985 900720, WO 90-EP1190 900720

FDT EP 485407 Al Based on WO 9101998; JP 04507241 W Based on WO 9101998 PRAI DE 89-3925183 890729

AN 91-044974 [07] WPIDS

AB DE 3925183 A UPAB: 930928

The TNF derivative (A) has the following amino acid sequence. Met(a) Val(b) Arg(c) Ser(d)-X(e)-Val(f) Arg(g) Ser(h) Arg(i) Thr Pro Ser Asp \*\*\*Lys\*\*\* \*\*\*Pro\*\*\* \*\*\*Val\*\*\* Ala His Val Val Ala Asn Pro Gln Ala Glu Gly Gln Leu Gin Trp Leu Asn Arg Arg Ala Asn Ala m Leu Leu Ala Asn Gly Val Glu Leu Arg Asp Asn Gln Leu Val Val Pro Ser Glu Gly Leu Tyr Leu Ile Tyr Ser Gln Val Leu Phe Lys Gly Gln Gly Cys Pro Ser Thr His Val Leu Leu Thr His Thr Ile Ser Arg Ile Ala Val Ser Tyr Glnm Thr Lys Asn Leu Leu Ser Ala Ile Lys Ser Pro Cys Gln Arg Glu Thr Pro Glu Gly Ala Glu Ala Lys Pro Trp Tyr Glu Pro Ile Tyr Leu Gly Gly Val Phe Gln Leu Glu Lys Gly Asp Arg Leu Ser Ala Glu Ile Asn Arg Pro Asp Tyr Leu Asp Phe Ala Glu Ser Gly Glnm Val Tyr Phe Gly Ile Ilea Ala Leu.

a,b,c,f,g i = 0-1; d,h = 0-4; e = 1-4, preferably 1,2 or 3; X = a peptide fragment of the leukokinin heavy chain, with the amino acid sequence Y-Pro-Arg-Z; Y,Z = a direct bond or a sequence of 1-6 amino acids. X is preferably Thr Lys Pro Arg, Ala Lys Thr Lys Pro Arg Gln Gln, His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe, Gly Gln Pro Arg or Lys Ala Lys Gly Glnm Pro Arg Glu Pro Gln Val. Also claimed are DNA (I) encoding (A); a vector containing (I) and a host organism containing the vector, used for the production of (A).

USE/ADVANTAGE - The protein is useful for treating neoplastic (malignant) and autoimmune diseases and for the treatment and prophylaxis of infections, \*\*\*inflammation\*\*\* and transplant rejection reactions. The hybrid molecule enhances the ability of TNF to degranulate neutrophilic granulocytes and to form superoxide.

ABEQ EP 485407 A UPAB: 930928

The TNF derivative (A) has the following amino acid sequence: Met(a) Val(b) Arg(c) Ser(d)-X(e)-Val(f) Arg(g) Ser(h) ARg(i) Thr Pro Ser Asp \*\*\*Lys\*\*\* \*\*\*Pro\*\*\* \*\*\*Val\*\*\* Ala His Val Val Ala Asn Pro Gln Ala Glu Gly Gin Leu Gln Trp Leu Asn Arg Arg Ala Asn Ala Leu Leu Ala Asn Gly Val Glu Leu Arg Asp Asn Gln Leu Val Val Pro Ser Glu Gly Leu Tyr Leu Ile Tyr Ser Gln Val Leu Phe Lys Gly Gln Gly Cys Pro Ser Thr His Val Leu Leu Thr His Thr Ile Ser Arg Ile Ala Val Ser Tyr Gln Thr Lys Val Asn Leu Leu Ser Ala Ile Lys Ser Pro Cys Gln Arg Glu Thr Pro Glu Gly Ala Lys Pro Trp Try Glu Pro Ile Tyr Leu Gly Gly Val Phe Gln Leu Glu Lys Gly Asp Arg Leu Ser Ala Glu Ile Asn Arg Pro Asp Thr Leu Asp Phe Ala Glu Ser Gly Gln Val Tyr Phe Gly Ile Ile Ala

a.b.c.f.g.i = 0-1; d,h = 0-4; e = 1-4, preferably 1,2 or 3; X = a peptide fragment of the leukokinin heavy chain, with the amino acid sequence Y-Pro-Arg-Z; Y, Z = a direct bond on sequence of 1-6 amino acids, X is preferably Thr Lys Pro Arg, Ala Lys Thr Lys Pro Arg Gln Gln, His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe, Gly Gln Pro Arg or Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val. Also claimed as DNA (I) encoding (A); vector containing (I) and a host organism containing the vector, used for the prodn. of (A).

USAE/AVANTAGE - The protein is useful for treating neoplastic (malignant) and autoimmune diseases and for the treatment and prophylaxis of infections, \*\*\*inflammation\*\*\* and transplant rejection reactions. The hybrid molecule enchances the ability of

TNF to degranulate neutrophilic granulocytes and to form superoxide.

```
L13
     ANSWER 20 OF 30 USPATFULL
AN
       91:104114 USPATFULL
ΤI
       Method of detecting Kawasaki disease using anti-tumor necrosis
       antibody
       Yone, Kenji, Hino, Japan
IN
       Suzuki, Jun, Tokyo, Japan
       Tsunekawa, Noriyuki, Hino, Japan
       Kato, Arata, Sayama, Japan
       Nakamura, Satoshi, Hino, Japan
       Maseqi, Tsukio, Hino, Japan
       Kitai, Kazuo, Hino, Japan
       Ichikawa, Yataro, Tokorozawa, Japan
PΆ
       Teijin Limited, Osaka, Japan (non-U.S. corporation)
PI
       US 5075236 911224
       US 88-186078 880425 (7)
ΑI
       JP 87-100010 870424
PRAI
       JP 87-162233 870701
       JP 87-162234 870701
       JP 87-268218 871026
       JP 87-268219 871026
       Utility
DT
       Primary Examiner: Kepplinger, Esther L.; Assistant Examiner:
EXNAM
       Scheiner, Toni
       Wenderoth, Lind & Ponack
LREP
CLMN
       Number of Claims: 5
ECL
       Exemplary Claim: 1
       7 Drawing Figure(s); 4 Drawing Page(s)
DRWN
LN.CNT 931
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       A method of confirming the diagnosis of Kawasaki disease in a
AB
       patient which comprises assaying the patient's body fluid for the
       presence of elevated levels of a substance specifically bound by
       an anti-tumor necrosis factor monoclonal antibody.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
     ANSWER 21 OF 30 CA COPYRIGHT 1997 ACS
L13
AN
     113:232079 CA
     Preparation of peptides as tumor necrosis factor (TNF)
ΤI
     agonists-antagonists
     Boehm, Hans Joachim; Daum, Lothar; Haupt, Andreas; Schmied,
IN
     Bernhard; Walker, Nigel; Zechel, Johann Christian
     BASF A.-G., Fed. Rep. Ger.
PA
     Ger. Offen., 16 pp.
SO
     CODEN: GWXXBX
PΙ
     DE 3841767 A1 900613
     DE 88-3841767 881212
AΙ
DT
     Patent
LA
     German
OS
    MARPAT 113:232079
     X-A-B-E-Leu-Y [A = Glu, Pro, Gln; B = Gly, Glu, Asn, Asp; E = Gln,
AB
     Ser; X = GNHCHMCO, GNHCHMCOW, GRNHCHMCO, etc.; Y = Z, VNHCHQCOUZ,
     etc.; G = H, amino-protective group; Z = OH, NH2, carboxy-protective
     group; GZ = bond, CO(CH2) nNH; n = 1-12; R, U = peptide chains from
     1-5 naturally occurring amino acids; W = ***Lys*** - ***Pro***
     - ***Val*** -Ala-His-Val-Val-Ala-Asn-Pro-Gln-Ala, etc.; V =
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Gln-Trp-Leu-Asn-Arg-Arg-Ala-Asn-Ala-Leu-Leu-Ala, etc.; M, Q = H, CHMe2, Ph, (CH2)mT, indolylmethyl, etc.; T = OH, OMe, SMe, H2N, HO2C, etc.; m = 1-6; MQ = (CH2)cSS(CH2)d, etc.; c, d = 1-4] and their physiol. acceptable salts, cytotoxic peptides having also TNF-antagonistic activity, useful for the treatment of neoplastic and autoimmune disease, and for the prophylaxis and treatment of infections, \*\*\*inflammations\*\*\*, and transplanted tissue rejections (no data), were prepd. by the solid-phase peptide-coupling method. Thus, 1.2 g BOC-Leu-MBAH-resin (BOC = tert-butyloxycarbonyl; MBAH = 4-methylbenzhydrylamino) was coupled with 2 mmol of the appropriate BOC-amino acid in each step and the N-terminal of the peptide-resin conjugate was deprotected by CF3CO2H to give 1.49 g intermediate product. The crude peptide (0.75 g) was HF-cleaved from the resin and purified by gel-filtration and medium-pressure chromatog. to give 97 mg title peptide H-Pro-Gln-Ala-Glu-Gly-Gln-Leu-NH2.

HF-cleaved from the resin and purified by gel-filtration and medium-pressure chromatog. to give 97 mg title peptide H-Pro-Gln-Ala-Glu-Gly-Gln-Leu-NH2. L13 ANSWER 22 OF 30 WPIDS COPYRIGHT 1997 DERWENT INFORMATION LTD AN 90~186575 [25] WPIDS N90-145119 DNN DNC C90-080876 New tumour necrosis factor derived peptide(s) - for treating or TIpreventing neoplastic and auto-immune diseases, infection, \*\*\*inflammation\*\*\* and transplant rejection. DC B04 S03 IN BOHM, H J; DAUM, L; HAUPT, A; SCHMIED, B; WALKER, N; ZECHEL, J C PA (BADI) BASF AG; (BOEH-I) BOEHM H J CYC PΙ DE 3841755 A 900613 (9025)\* WO 9006938 A 900628 (9029) RW: AT BE CH DE ES FR GB IT LU NL SE W: JP US CA 2005056 A 900612 (9035) EP 447431 A 910925 (9139) R: AT BE CH DE ES FR GB IT NL JP 04502307 W 920423 (9223) 11 pp DE 3841755 A DE 88-3841755 881212; EP 447431 A EP 90-900108 891202; ADT JP 04502307 W WO 89-EP1471 891202, JP 90-500555 891202 JP 04502307 W Based on WO 9006938 FDT PRAI DE 88-3841755 881212 AN90-186575 [25] WPIDS AB DE 3841755 A UPAB: 951102 Peptides of formula (I) and their physiologically tolerable acid salts are new: X-Ala-His-A-Y (I) A = Val, Leu, Ile or NH(CH2)mCO; m = 1-2; X = G-NH-CHM-CO, G-NH-CHM-CO-W, G-R-NH-CHM-CO or G-R-NH-CHM-CO-W; Y = Z, NH-CHQ-COZ, V-NH-CH1-COZ, NH-CHQ-CO-U-Z or V-NH-CHQ-CO-U-Z; G=H or amino protecting gp.; Z=OH, NH2 or carboxy protecting gp.; R = Leu-Arg(Ser)3Gln Asn(Ser)2Asp-\*\*\*Lvs\*\*\* - \*\*\*Pro\*\*\* \*\*\*Val\*\*\* -Arg(Ser)3 Arg-Thr-Pro-Ser-Asp-Lys-Pro; Leu-Arg(Ser)3Gln -Ala(Ser)2Asn-Lys-Pro; Leu-Arg-Ser-Ala-Ser-Arg-Ala-Leu-Ser-Asp-Lys-Pro (or a 5-11 amino acid fragment of the sequences) or a peptide chain with 1-4 naturally occurring alpha amino acids; U, V and W = peptide chains with 1-4 naturally occurring alpha amino acids; M and Q = H, isopropyl, CHMe.Et, phenyl, CH(OH).Me, 3-indolyl methyl, 4-imidazolylmethyl or (CH2)bT; b = 1-6; T = OH, Ome, SMe, isopropyl, phenyl (opt. 4-substd. by OH), SH, NH2, COOH, CONH2 or NH2.C(NH).NH; or Me and Q are together (CH2)c:S-S(CH2)d, (CH2CONH)ef or (CH2) c and d = 1-4; e and f = 1-6; g = 1-12.

USE - (I), which are low mol.wt. derivs. of tumour necrosis factor (TNF), are useful for treating neoplastic and autoimmune diseases, and for treating or preventing infection, \*\*\*inflammatory\*\*\* and transplant rejection reactions. Some have cytotoxic activity while others have high affinity for cellular TNF receptor, without being cytotoxic. These cpds. are thus antagonists of TNF. @(17pp Dwg.No.0/0)

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L13 ANSWER 23 OF 30 USPATFULL
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AN 89:85895 USPATFULL

TI Method of using melanocyte stimulating hormone as dermatis treatment

IN Nordlund, James J., Cincinnati, OH, United States Rheins, Lawrence A., Cincinnati, OH, United States

PA University of Cincinnati, Cincinnati, OH, United States (U.S. corporation)

PI US 4874744 891017

AI US 89-323606 890313 (7)

DT Utility

EXNAM Primary Examiner: Lee, Lester L.

LREP Wood, Herron & Evans
CLMN Number of Claims: 9
ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 214

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

Dermatitis is treated by topically applying a composition including melanocyte stimulating hormone to the epidermal portion of the infected skin. Preferably, alpha-melanocyte stimulating hormone is applied in a concentration in the range of about 5.times.10.sup.-5 M/cm.sup.2. This is an effective treatment against a broad range of dermatitis. Occlusion of the affected site enhances response.

#### CAS INDEXING IS AVAILABLE FOR THIS PATENT.

- L13 ANSWER 24 OF 30 CA COPYRIGHT 1997 ACS
- AN 111:187865 CA
- TI Antiinflammatory activity of a carboxy-terminal fragment of the neuropeptide .alpha.-MSH
- AU Hiltz, Melanie E.; Lipton, James M.
- CS Southwest. Med. Cent., Univ. Texas, Dallas, TX, 75235, USA
- SO FASEB J. (1989), 3(11), 2282-4 CODEN: FAJOEC; ISSN: 0892-6638
- DT Journal
- LA English
- AB Preliminary research has indicated that the C-terminal tripeptide of .alpha.-MSH ( \*\*\*Lys\*\*\* \*\*\*Pro\*\*\* \*\*\*Val\*\*\* ) inhibited increases in vasopermeability, raising the possibility that this portion of the .alpha.-MSH mol. has general antiinflammatory activity. To test this idea, the effects of graded doses of .alpha.-MSH [11-13] on ear swelling induced by picryl chloride in mice were compared with the effects of saline and a large dose of corticosteroid; .alpha.-MSH [11-13] inhibited swelling in a dose-related fashion. This result, together with previous findings, suggests that endogenous circulating .alpha.-MSH and its C-terminal fragments may contribute to modulation of physiol. responses in host

defense. If this is true, it may be possible to develop new peptide drugs or mimetics based on the tripeptide that are useful in treating \*\*\*inflammation\*\*\* .

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DUPLICATE 2
    ANSWER 25 OF 30 CA COPYRIGHT 1997 ACS
L13
     110:109081 CA
AN
     Antipyretic and anti- ***inflammatory*** peptides
TI
     Lipton, James M.
IN
     University of Texas System, USA
PA
     PCT Int. Appl., 29 pp.
SO
     CODEN: PIXXD2
                   880211
     WO 8800833 A2
PΙ
         AT, AU, BB, BG, BR, CH, DE, DK, FI, GB, HU, JP, KP, KR, LK, LU,
DS
         MC, MG, MW, NL, NO, RO, SD, SE, SU
     RW: AT, BE, BJ, CF, CG, CH, CM, DE, FR, GA, GB, IT, LU, ML, MR, NL,
         SE, SN, TD, TG
     WO 87-US1994 870807
ΑI
PRAI US 86-894910 860808
     US 87-76625 870723
     Patent
DT
     English
LA
       ***Lys*** - ***Pro*** - ***Val*** and its N-acylated and
AB
     amidated derivs. are prepd. for reducing fever and
     ***inflammation*** in mammals. They are esp. effective in
     combination with Cu salts. Fever was induced in rabbits by i.v.
     injection of leukocytic pyrogen (produced by incubating leukocytes
     with Salmonella typhosa endotoxin). The fever was reduced 67% by i.v. injection of 200 mg ***Lys*** - ***Pro*** - ***Val***
     (duration of action 1.5 h) and >50% by i.v. injection of 0.5 mg
               ***Lys*** - ***Pro*** - ***Val*** -NH2 (I) (duration
     of action .gtoreq.4 h). CuCl2, administered centrally or
     peripherally, greatly augmented the action of I. The soln.-phase
     synthesis of di(benzyloxycarbonyl)lysylprolylvaline benzyl ester and
     its deprotection and conversion to I are described.
                              COPYRIGHT 1997 DERWENT INFORMATION LTD
     ANSWER 26 OF 30 WPIDS
L13
     87-235291 [33]
                      WPIDS
AN
     C87-099398
DNC
     Stimulating skin levels of melanin - by topical administration of
TI
     alpha melanocyte stimulating hormone.
     B04 D18 D21
DC
     CODY, W L; DORR, R; HADLEY, E M; HRUBY, J V; LEVINE, N; SUGG, E;
IN
     HADLEY, M E; HRUBY, V J
      (UYPA) UNIVERSITY PATENTS INC; (HRUB-I) HRUBY V J
PA
CYC
     WO 8704623 A 870813 (8733) * EN
ΡI
        RW: AT BE CH DE FR GB IT LU NL SE
          W: AU DK HU JP KR RO SU
      AU 8770828 A 870825 (8745)
      DK 8705181 A 871202 (8811)
                 A 880316 (8811)
      EP 259440
         R: AT BE CH DE FR GB IT LI LU NL SE
      JP 63502894 W 881027 (8849)
      US 4866038 A 890912 (8946)
      US 4918055 A 900417 (9020)
      CA 1282324 C 910402 (9118)
      US 5049547 A 910917 (9140)#
      KR 9005903 B 900816 (9142)
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B1 930113 (9302) EN
         R: AT BE CH DE FR GB IT LI LU NL SE
     DE 3783541 G 930225 (9309)
     NZ 233248
                 A 930127 (9310)
     JP 06011710 B2 940216 (9410)
                                         7 pp
     EP 259440
                 A4 891227 (9509)
     WO 8704623 A WO 87-US226 870123; EP 259440 A EP 87-901815 870123; JP
     63502894 W JP 87-501451 870123; US 4918055 A US 88-154823 880211; US
     5049547 A US 89-340305 890419; EP 259440 B1 EP 87-901815 870123, WO
     87-US226 870123; DE 3783541 G DE 87-3783541 870123, EP 87-901815
     870123, WO 87-US226 870123; NZ 233248 A NZ 87-233248 870203; JP
     06011710 B2 JP 87-501451 870123, WO 87-US226 870123; EP 259440 A4 EP
     87-901815
     EP 259440 B1 Based on WO 8704623; DE 3783541 G Based on EP 259440,
     Based on WO 8704623; NZ 233248 A Div ex NZ 219158; JP 06011710 B2
     Based on JP 63502894, Based on WO 8704623
                    860203; US 88-224187
PRAI US 86-825162
     87-235291 [33]
                      WPIDS
     WO 8704623 A
                    UPAB: 930922
     Melanin prodn. is stimulated in mammal melanocytes by topical
     administration of alpha-melanocyte stimulating hormone which is a
     tridecapeptide of formula (I) or analogues of (I)
          Ac-Ser-Tyr-Ser-Met-Glu -His-Phe-Arg-Trp- Gly- ***Lys***
     ***Pro*** - ***Val***
                             -NH2 (I).
          Pref. (I) and analogues are disclosed in US4457864 and 4485039
     and are of the formula (Ia):- R1-W-X-Y-Z-R2 (Ia); R1 is Ac-Gly-,
     Ac-Met-Gln-, Ac-Nle-Glu-, Ac-Tyr-Glu-; W is His or D-His; X is Phe.
     D-Phe, Tyr, D-Tyr, p-nitro-D-Phe; Y is Arg, D-Arg; Z is Trp or
     D-Trp; R2 is NH2, Gly-NH2 or Gly-Lys-NH2. p-nitro-Phe is
     p-nitrophenylalanine. All amino acid residues are in L
     configuration unless specifically indicated as D.
          USE - (I) and its derivs. are used in the transdermal treatment
     of hypopigmentation dysfunctions e.g. post- ***inflammatory***
     hypopigmentation, pityriasis alba, tinea versiocolour, vitiligo,
     idiopathic guttate hypomellanosis and nevus depigmentosus. They can
     also be used to darken grey hair caused by ageing, darken animal
     pelts and form sun-tanning in the absence of sun or UV light.
     0/0
ABEO EP 259440 B
                    UPAB: 930922
     A method for tanning the skin, which comprises applying topically to
     the skin, in an amount sufficient to cause stimulation of
     non-follicular melanocytes, a compound selected from: (1) alpha-MSH
     having the amino acid formula (I); (2) alpha-MSH analogues having
     the formula (II); wherein M is selected from Met and Nle: (3)
     analogues of alpha-MSH having the formula: R1-W-X-Y-Z-R2 (III),
     wherein R1 is selected from Ac-Gly, Ac-Met-Glu, Ac-Nle-Glu and
     Ac-Tyr-Glu; W is selected from His and D-His; X is selected from
     Phe, D-Phe, Tyr, D-Tyr and (pNO2)D-Phe; Y is selected from ARg and
     D-Arg; Z is selected from Trp and D-Trp; and R2 is selected from
     NH2, Gly-NH2 and Gly-Lys-NH2; and (4) alpha-MSH analogues selected
          (Nle4, D-Phe7) -alpha-MSH; (Nle4, D-Phe7) -alpha-MSH4-10; (Nle4,
    D-Phe7) -alpha-MSH4-11; (Nle4, D-Phe7, D-Trp3) -alpha-MSH4-11; (Nle4,
     D-Phe7)-alpha-MSH4-9; (Cys4, Cys10)-alpha-MSH; (Cys4,
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Cys10)-alpha-MSH4-12; (Cys4, Cys11)-alpha-MSH; (Cys5, Cys10)-alpha-MSH; (Cys5, Cys11)-alpha-MSH; and (Cys4,

Cys10) -alpha-MSH4-13.

0/0

ADT

FDT

ΑN

AΒ

ABEQ US 4866038 A UPAB: 930922 New method of stimulating melanin prod. by integumental melanocytes comprises admin. (usually topically) alpha melanocyte stimulating hormone (alpha-MSH) of formula Ac-Ser-Tyr-Ser-Met-Glu-His-Phe-Arg-Trp- Gly-Lis-Pro-Val-NH2, or various specified analogues with modified individual amino acids or part sequence. USE - Treatment of hypopigmentation dysfunctions and tanning of skin or darkening of grey hair caused by lack of enzyme. The pigmentation induced prevents UV damage to skin. UPAB: 930922 ABEQ US 4918055 A Process for stimulating melanocytes and the formation of melanin comprises admin. of alpha-melanotropin of formula Ac-Ser-Tyr-Ser-M-Glu -His-Phe-Arg-Trp-Gly- \*\*\*Lys\*\*\* - \*\*\*Pro\*\*\* - \*\*\*Val\*\*\* -NH2 (where M is -Met-) and/or its analogues (where M is Met, Nle or Cys and D-Phe is present instead of L-Phe) and/or related peptides or their derivs., dispersed with the usual carriers and opt. additives. USE - The prods. promote the secretion of melanin into hair and skin, restoring hair colour and giving a tanning effect without resource to u.v. radiation and its associated hazards. ABEQ US 5049547 A UPAB: 930922 Pharmaceutical compsn. comprises 1 or more active components (a) alpha-MSH of formula Ac-Ser-Tyr-Ser-Met-Glu-His-Phe-Arg-Trp-Gly-\*\*\*Lys\*\*\* - \*\*\*Pro\*\*\* - \*\*\*Val\*\*\* -NH2; (b) its analogue Ac-Ser-Tyr-Ser-M-Glu-His-D-Phe-Arg-Trp-Gly- \*\*\*Lys\*\*\* -NH2; (c) analogue R1-W-X-Y-ZR2; or (d) analogue (Nle4, D-Phe7) alpha-MSH, (Nle4, D-Phe7) alpha-MSH 4-10, (Nle4, D-Phe7)alpha-MSH4-11, (Nle4, D-Phe7, D-Trp9)-alpha-MSH4-11, or (Nle4, D-Phe7)-alpha-MSH4-9. M is Met, Nle, or Cys; R1 is Ac-Gly, Ac-Met-Glu, Ac-Nle-Glu, or Ac-Tyr-Glu; W is His or D-His; X is Phe, D-Phe, Tyr, D-Tyr, or (pNO2) D-Phe; Y is Arg or D-Arg; Z is Trp or D-Trp; and R2 is NH2, Gly-NH2, or Gly-Lys-NH2. USE - To produce melanin in a vertebrate in a compsn. contg. pharmaceutical carrier to stimulate melanin prodn. upon administration. ANSWER 27 OF 30 USPATFULL L13 AN 77:19596 USPATFULL TINovel polypeptides having ACTH-like action ΙN Inouye, Ken, Kobe, Japan Shin, Masaru, Kobe, Japan Watanabe, Kunio, Otsu, Japan PA Shionogi & Co., Ltd., Osaka, Japan (non-U.S. corporation) PΙ US 4018754 770419 AΙ US 75-596246 750716 (5) PRAI JP 74-87758 740730 DTUtility EXNAM Primary Examiner: Gotts, Lewis; Assistant Examiner: Suyat, Reginald J. Wenderoth, Lind & Ponack LREP Number of Claims: 5 CLMN ECLExemplary Claim: 1 DRWN 2 Drawing Figure(s); 2 Drawing Page(s) LN.CNT 608

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

A polypeptide of the formula:

AΒ

X.sub.1 --Tyr--Ser--X.sub.2 --X.sub.3 --His--Phe--Arg--Trp--Gly-\*\*\*Lys\*\*\* -- \*\*\*Pro\*\*\* -- \*\*\*Val\*\*\* --Gly--(Lys).sub.n --Y

wherein X.sub.1 is .alpha.-aminoisobutyric acid, .beta.-alanine, L-serine, D-serine, glycine, D-alanine, .gamma.-aminobutyric acid or sarcosine residue; X.sub.2 is L-methionine, L-norleucine, L-isoleucine or L-norvaline residue; X.sub.3 is L-glutamic acid or L-glutamine residue; n is an integer of 5-10; and Y is --R.sub.1, ##STR1## wherein R.sub.1 is hydroxy or lower alkoxy having 1-5 carbon atoms; R.sub.2, R.sub.3, R.sub.4 and R.sub.5 are each hydrogen or lower alkyl having 1-5 carbon atoms; m is an integer of 1-10 and Y is a group bound to the carbonyl group of the C-terminal lysine residue; non-toxic acid addition salts thereof; and complexes thereof; being useful as a medicament owing to their strong adrenal-stimulating activity with protracted action and little side effects. They can be prepared by condensing the amino acids together one by one or by condensing the small peptide fragments together in a per se conventional manner.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

```
ANSWER 28 OF 30 USPATFULL
L13
       77:19595 USPATFULL
AN
       Polypeptides with ACTH-like activities
TI
       Inouye, Ken, Kobe, Japan
IN
       Shin, Masaru, Kobe, Japan
       Watanabe, Kunio, Otsu, Japan
       Shionogi & Co., Ltd., Osaka, Japan (non-U.S. corporation)
PA
       US 4018753 770419
PΙ
       US 75-596245 750716 (5)
ΑI
       JP 74-87759 740730
PRAI
       Utility
DT
      Primary Examiner: Gotts, Lewis; Assistant Examiner: Suyat,
FXNAM
       Reginald J.
       Wenderoth, Lind & Ponack
LREP
       Number of Claims: 4
CLMN
       Exemplary Claim: 1
ECL
       No Drawings
DRWN
LN.CNT 779
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       A polypeptide of the formula:
AB
```

X.sub.1 -Tyr-Ser-X.sub.2 -X.sub.3 -His-Phe-Arg-Trp-Gly- \*\*\*Lys\*\*\*
- \*\*\*Pro\*\*\* - \*\*\*Val\*\*\* -Gly-(Lys).sub.n -Y

wherein X.sub.1 is .alpha.-aminoisobutyric acid, .beta.-alanine, L-serine, glycine, D-serine, D-alanine, .gamma.-aminobutyric acid or sarcosine residue; X.sub.2 is L-methionine, L-norleucine, L-isoleucine or L-norvaline residue; X.sub.3 is L-glutamic acid or L-glutamine residue; n is an integer of 1-4 and Y is a group of ##STR1## which is linked to the carbonyl group of the C-terminal lysine residue, wherein R.sub.1 and R.sub.2 are each hydrogen or the same or different lower alkyl having 1-5 carbon atoms, and R.sub.1 and R.sub.2, when taken together with or without another hetero atom, form a substituted or unsubstituted nitrogen containing heterocyclic ring, with the proviso that a peptide when X.sub.1 is a .alpha.-aminoisobutyric acid or D-serine, R.sub.1 and R.sub.2 are each hydrogen and n is 4 is excluded; non-toxic acid

addition salts thereof and complexes thereof; being useful as a medicament owing to their strong adrenal-stimulating activity with protracted action and little side effects. They can be prepared by condensing the amino acids together one by one or by condensing the small peptide fragments together in a per se conventional manner.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

PRAI JP 74-87758

740730

```
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    ANSWER 29 OF 30 WPIDS
L13
     76-13404X [08]
                     WPIDS
AN
     Adrenocorticotrophic polypeptides having prolonged activity - with
TΤ
     lower melanocyte-stimulating effect.
     B05 C03
DC
     (SHIO) SHIONOGI & CO LTD
PA
CYC
     DE 2534086 A 760212 (7608)*
PΙ
    NL 7508927 A 760203 (7608)
     JP 51016667 A 760210 (7613)
     FR 2280388 A 760402 (7621)
     US 4018753 A 770419 (7717)
     GB 1513472 A 780607 (7823)
     CH 612917 A
                   790831 (7938)
PRAI JP 74-87759
                   740730
     76-13404X [08]
                     WPIDS
AN
     DE 2534086 A UPAB: 930901
AB
     Polypeptides of formula (I) and their acid salts and complexes are
     new: X1-Tyr-Ser-X2-X3-His-Phe-Arg-Yrp-Gly- ***Lys*** - ***Pro***
        ***Val*** -Gly(Lys)n-Y (I) (X1 = alpha-aminoisobutyric acid
     (Aib), beta-alanine, L- or D-serine, glycine, D-alanine,
     gamma-aminobutyric acid or sarcosine; X2 = L-methionine,
     L-norleucine, L-isoleucine or L-norvaline; X3 = L-glutamic acid or
     L-glutamine; n = 1-4 and Y (attached to CO of the C-terminal lysine)
     is NR1R2; R1 and R2 are each H or 1-5C alkyl or together with N
     complete a heterocycle which can be substd. and/or include other
     heteroatoms. Cpds. with X1 = Aib or D-Ser; R1=R2=H and n = 4, are
     excluded). (I) have prolonged and strong adrenal-stimulating
     activity but only a weak melanocyte-stimulating effect. They can be
                    ***inflammation*** , adrenal insufficiency caused
     used to treat
     by hypophysical disorders, acute and chronic articular rheumatism
     and allergies, and also to investigate adrenal function in humans or
     animals.
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     ANSWER 30 OF 30
L13
                     WPIDS
     76-13403X [08]
                     WPIDS
AN
     Adrenocorticotropic polypeptides with polylysyl gp. at the C-end -
ΤI
     to improve and prolong activity and reduce melanocyte stimulation.
DC
     B04 C03
     (SHIO) SHIONOGI & CO LTD
PA
CYC
     7
                   7.60212 (7608) *
PΙ
     DE 2534085 A
     NL 7508932 A 760203 (7608)
     JP 51016666 A 760210 (7613)
     FR 2280389 A 760402 (7621)
     US 4018754 A 770419 (7717)
     GB 1516725 A 780705 (7827)
     CH 612918 A
                   790831 (7938)
```

AN 76-13403X [08] WPIDS AB DE 2534085 A UPAB: 930901

= >

Polypeptides of formula (I) and their acid salts and complexes are new: X1-Tyr-Ser-X2-X3-His-Phe-Arg-Trp-Gly- \*\*\*Lys\*\*\* - \*\*\*Pro\*\*\* - \*\*\*Val\*\*\* -Gly-(Lys)n-Y(I) (X1 = an alpha-aminoisobutyric acid (Aib), beta-alanine, D- or L-serine, glycine, D-alanine, gamma-aminobutyric acid or sarcosine residue; X2 = L-methionine, L-norleucine, L-isoleucine or L-norvaline; X3 = L-glutamic acid or L-glutamine; n = 5-10; Y = NR2R3, NH-(CH2)mNR4R5, OH or 1-5C alkoxy bonded to the carbonyl gp. of the final lysine residue; R2,R3,R4 and R5 = H or 1-5C alkyl; m = 1-10). (I) have ACTH activity superior to that of the natural hormone but have only mild melanocyte-stimulating action.

They provide a long-term effect even when not in the form of a complex and are useful in treatment of \*\*\*inflammation\*\*\* , adrenal disease or insufficiency, hypophyseal disorders, chronic or acute articular rheumatism and allergies, and to investigate adrenal gland function in humans or animals.